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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/574,460	05/18/2000	Michael A. Apicella	875.009US1	6817

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EXAMINER
PAK, YONG D

ART UNIT	PAPER NUMBER
1652	13

DATE MAILED: 03/13/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/574,460	APICELLA ET AL.	
	Examiner	Art Unit	
	Yong Pak	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 January 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *6-8,11,12 and 18-21* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *6-8,11,12 and 18-21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *12* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

The amendment filed on January 2, 2002, canceling claims 1,5, 9, 14, 16 and 17, amending claims 6-8, 11 and 12 and adding claims 18-21, has been entered.

Claims 6-8, 11-12 and 18-21 are pending.

Declaration

The declaration under 37 CFR 1.132 filed January 2, 2002 is sufficient to overcome the rejection of claims 6-8, 11-12, 14 and 18-21 based upon 35 USC § 112, 1st paragraph made in Paper No. 8.

The text of those sections of Title 35 U.S. Code not included in this action can be found in a prior Office action. Rejections and/or objections not reiterated from previous Office action are hereby withdrawn.

Claim Rejections - 35 USC § 112

Claims 8, 11-12 and 20-21 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 8, 11-12 and 20-21 are drawn to a process of producing oligosaccharides or carbohydrates in bacteria encoding rfe (UDP-GlcNAc:Undecaprenol GlcNAc-1 phosphate transferase) from any source and. These claims comprise a vast diverse

genus of rfe enzymes. Although claim 12 limits claim 11 to a rfe enzyme from *Haemophilus influenzae,* art nor the specification describe a rfe from *H. influenzae* to use in the claimed method. The specification only describes producing oligosaccharides, as represented in Figure 3, in Escherichia coli K-12 transformed with *rfe*, a UDP-GlcNAc: Undecaprenol GlcNAc-1 phosphate transferase from *E. coli* and a lipooligosaccharide-synthesis gene (*lsg*) from *H. influenzae*. Therefore, the specification describes one representative species of a diverse genus.

Given this lack of the description of the representative species encompassed by the genus of the claims used in the method of sialylating glycoproteins, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicants were in possession of the inventions of claims 8, 11-12 and 20-21.

Claim 8, 11-12 and 20-21 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for producing lipooligosaccharides with *E. coli* rfe, does not reasonably provide enablement for producing oligosaccharides in with a rfe enzyme different from the *E. coli* rfe. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

The specification gives inadequate guidance in producing oligosaccharides with any rfe. Applicants teach production of oligosaccharides, as represented in Figure 3, with *E. coli* K-12 cells expressing a rfe enzyme from E. coli. To practice the invention,

the rfe enzyme must be known. However, the specification only teaches a rfe from E. coli and neither art nor the specification teaches a rfe from H. influenzae.

Despite knowledge in the art for the isolation of amino acids, the specification fails to provide guidance regarding how to isolate other rfe whose sequence is different from the rfe of *E. coli*. Therefore, the breadth of these claims is much larger than the scope enable by the specification.

The predictability as to the level of conservation between the disclosed sequences and those of other rfe is complex. While recombinant techniques are available, it is not routine in the art to screen large numbers of amino acids where the expectation of obtaining similar sequences is unpredictable. The amino acid sequence determines the structural and functional properties of an enzyme. Knowledge of which sequences can be altered or removed and still result in similar protein activity is well outside the realm of routine experimentation.

Therefore, one of ordinary skill would require guidance to produce lipooligosaccharides with rfe different from the rfe of *E. coli*. Without such guidance, the experimentation left to those skilled in the art is undue.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 6-8, 11-12, 18-19 and 21are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 6-8 recite the limitation "claim 11" in line 1. There is insufficient antecedent basis for this limitation in the claim.

In claims 11-12, 18-19 and 21, the phrase "DNA sequence encoding a lipooligosaccharide-synthesis gene (lsg)" is confusing because a DNA sequence does not encode a gene.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 6-8, 11-12 and 18-21 are rejected under 35 U.S.C. 103(a) as being unpatentable over McLaughlin et al. in view of Alexander et al.

McLaughlin et al. (form PTO-1449) teach a process for production of H. influenzae-specific lipooligosaccharides (or complex carbohydrates) using a lipooligosaccharide-synthesis gene (lsg) from H. influenzae (pages 166-167). McLaughlin et al. teach that the various sugar transferases express from the lsg are responsible for the modification of the existing E. coli LPS (page 172). McLaughlin et al. also teach that the lipooligosaccharides of H. influenzae are important virulence factors for this pathogen.

The difference between the reference of McLaughlin et al. and the instant invention is that the reference of McLaughlin et al. does not teach a process of making the lipooligosaccharide using a rfe enzyme.

Alexander et al. (form PTO-1449) teach an *E. coli* rfe and that the enzyme is essential for the first step in the biosynthesis of lipooligosaccharide (page 7079). Therefore, it would have been obvious to one having ordinary skill in the art at the time the claimed invention was made to make lipooligosaccharides with a *E. coli* K-12 expressing an *E. coli* rfe and a H. influenzae lsg. The motivation of making *H. influenzae*-specific lipooligosaccharides is to produce the lipooligosaccharide in large amounts to effectively obtain oligosaccharides, useful in developing vaccines and in identification of the *H. influenzae* bacteria itself. One of ordinary skill in the art would have had a reasonable expectation of success since recombinant technology is performed routinely in the art.

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within

TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Yong Pak whose telephone number is 703-308-9363. The examiner can normally be reached on 8:00 A.M. to 4:30 P.M weekdays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on 703-308-3804. The fax phone numbers for the organization where this application or proceeding is assigned are 703-872-9310 for regular communications and 703-746-7240 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Yong Pak
Patent Examiner

March 7, 2002

PONNATHAPU ACHUTAMURTHY
SUPERVISORY PATENT EXAMINER
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